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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,435	11/26/2003	Weihong Xiong	01121-17272	6215

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

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11/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,435	XIONG ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2007* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-84, 86-103* is/are pending in the application.

4a) Of the above claim(s) *53-80,87-97,99 and 101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *81-84,86,98,100,102 and 103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 02/15/2007, election filed 06/21/2007, and amendment and declaration both filed 08/30/2007.

Election/Restrictions

1. Applicant's election without traverse of Group I claims 81-84, 86, 98, 100, 102 and 103 in the reply filed on 06/21/2007 is acknowledged.

2. Claims 53-80, 87-97, 99, 101 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups I, and II, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/21/2007.

Claims 81-84, 86, 98, 100, 102, and 103 are included in the prosecution.

The following rejections have been overcome by virtue of applicants' amendment and remarks:

(A) The rejection of claims 82, 87-97 under 35 U.S.C. 112, second paragraph, as being indefinite.

(B) The rejection of claims 81-86, 90, 93-97 under 35 U.S.C. 103(a) as being unpatentable over US 6,159,986 ('986).

(C) The rejection of claims 81, 83-86 under 35 U.S.C. 103(a) as being unpatentable over CN 1111987 ('987).

(D) The rejection of claim 82 under 35 U.S.C. 103(a) as being unpatentable over CN '987 in view of US '715.

(E) The rejection of claims 90, and 93-97 under 35 U.S.C. 103(a) as being unpatentable over any of US '715 or CN '987 in view of US '986.

(F) The rejection of claims 87-89 under 35 U.S.C. 103(a) as being unpatentable over any of US '715, US '986 or CN '987 each in view of US 6,524,616 ('616).

(G) The rejection of claims 87-90, 94, 95 and 97 under 35 U.S.C. 103(a) as being unpatentable over any of US '715 or CN '987 each in view of the article "Drug Treatment for Alzheimer's Disease" by Tiffany et al.

(H) The rejection of claims 87-89 under 35 U.S.C. 103(a) as being unpatentable over US '986 in view of Tiffany et al.

(I) The rejection of claims 90 and 93 under 35 U.S.C. 103(a) as being unpatentable over any of US '715 and CN '987 each in view of 5,104,880 ('880).

(J) The rejection of claims 90 and 91 under 35 U.S.C. 103(a) as being unpatentable over US '715 and CN '987 each in view of US 5,877,173 ('173).

(K) The rejection of claim 91 under 35 U.S.C. 103(a) as being unpatentable over US '986 in view of US '173.

(L) The rejection of claims 90-92 under 35 U.S.C. 103(a) as being unpatentable over any of US '715 or CN '987 each in view of US 5,668,117 ('117).

(M) The rejection of claims 91 and 92 under 35 U.S.C. 103(a) as being unpatentable over US '986 in view of US '117.

The following new ground of rejections are necessitated by applicants' amendment:

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 81-84, 86, 98, 100, 102, 103 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 81 recites "acrylate polymer or rubber-based pressure sensitive adhesive including homopolymers, copolymers and terpolymers thereof". Recourse to the specification applicants did not disclose any homopolymers, copolymers and terpolymers of rubber-based adhesive.

Additionally, claim 100 recites that the permeation enhancer is "lauryl lactate". Recourse to the specification, nowhere applicants disclosed "lauryl lactate" as permeation enhancer.

In accordance to MPEP 714.02, applicant should specifically point out to where in the disclosure a support for any amendment made to the claims can be found.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 81-84, 86, 98, 100, 102, and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US 6,352,715 ('715) with the effective filing date February 19, 1998 in view of US 6,26,063 ('063) with the effective filing date May 27, 1999.

US '715 teaches a transdermal drug delivery system to administer huperzine A in a controlled release skin patch designed for once-a-week application to treat Alzheimer disease (AD) (abstract; col.3, lines 55-65; col.4, lines 7-15; col.9, lines 1-7, 31). The patch comprises polyacrylate adhesive layer containing huperzine (col.9, lines 32-35; col.14, lines 65-67). The reference suggests the use of co-solvents to increase skin permeability of huperzine A (col.8, lines 65-67).

However, US '715 does not teach the blood plasma levels of huperzine provided by the transdermal system as instantly claimed.

The blood plasma levels are controlled by the amount of the drug included in the system as well as by the ingredients of the transdermal formulation used to deliver the huperzine such as the type of the adhesive, the permeation enhancers and other additives in the formulation.

Therefore, the claimed blood plasma levels of huperzine can be determined by one having ordinary skill in the art by manipulating the transdermal formulation containing the huperzine and the structure of the transdermal device delivering it. Additionally, individual patient-need is also a controlling factor in determination of the dose of huperzine.

It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller,* 105 USPQ 233.

US '063 teaches topical application of muscarinic agents including huperzine (abstract; col.3, line 2). The reference teaches that the drug can be combined with enhancing agent to enhance the penetration of the drug into the skin and suitable enhancers include fatty acid and fatty acid esters such as oleic acid, lauric acid, and lauryl lactate, and azone (col.5, lines 36-55, col.6, lines 1-6).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery system to deliver huperzine to treat patients suffering from AD wherein the system comprises polyacrylate adhesive and may contain permeation enhancer as disclosed by US '715, and add a permeation enhancer including fatty acid or fatty acid ester that are disclosed by US '063 to enhance the delivery of huperzine into the skin, with reasonable expectation of having a transdermal delivery system to treat AD comprising huperzine in polyacrylate adhesive and permeation enhancer selected from fatty acids or fatty acid esters that enhance the delivery of the huperzine into the skin successfully, and additionally one having ordinary skill in the art would have been motivated to manipulate the amount of huperzine and the formulation containing it, as well as the structure of the transdermal delivery system motivated by the specific individual patient need to achieve the desired results, with reasonable expectation of having transdermal delivery system that provides the desired

blood plasma levels of huperzine for extended time to treat the AD patients with great success.

8. Claims 81, 83, 84, 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over CN 1111987 ('987) in view of US '063.

CN '987 teaches a plaster for treating senile dementia with long activity life of 3-4 days comprising huperzine (abstract). CN '987 teaches the plaster containing adhesive layer containing 0.1 to 8% w/w of huperzine, and applicants used in all their examples 0.01 to 20% w/w of huperzine. Therefore, it is expected that the same amount of huperzine disclosed by the prior art to provide the same blood plasma level of huperzine if it is present in the same formulation. The reference teaches permeation enhancer, however, does not specifically teach the claimed enhancer.

US '063 teaches permeation enhancer including fatty acids, fatty esters and azone (col.5, lines 35-55; col.6, lines 1-3).

Therefore, the art recognized the equivalency between fatty acids and their esters and azone as a penetration enhancer of huperzine into the skin.

CN '987 does not teach explicitly teach the blood plasma levels of huperzine provided by the transdermal system as instantly claimed, however, it is expected that the plaster disclosed by CN '987 to provide the same blood plasma level of huperzine because it contains the same amount of the huperzine. The plasma levels are controlled by the amount of huperzine included in the system as well as by the ingredients of the

transdermal formulation used to deliver the huperzine such as the type of the adhesive, the permeation enhancers and other additives in the formulation.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery system to deliver huperzine to treat patients suffering from AD wherein the system comprises adhesive and permeation enhancer as disclosed by CN '987, and replace the permeation enhancer disclosed by CN '987 by enhancer including fatty acid or fatty acid ester that are disclosed by US '063 to enhance the delivery of huperzine into the skin since azone is known to cause skin irritation as admitted by applicant, at page 20 of their disclosure, and since the art recognized the equivalency between fatty acids an their esters and azone in terms of enhancing huperzine delivery into the skin, with reasonable expectation of having a transdermal delivery system to treat AD comprising huperzine in adhesive and permeation enhancer selected from fatty acids or fatty acid esters that enhance the delivery of the huperzine into the skin without skin irritation successfully, and additionally one having ordinary skill in the art would have been motivated to manipulate the amount of huperzine and the formulation containing it, as well as the structure of the transdermal delivery system motivated by the specific individual patient need to achieve the desired results, with reasonable expectation of having transdermal delivery system that provides the desired blood plasma levels of huperzine for extended time to treat the AD patients with great success.

Response to Arguments

9. Applicant's arguments with respect to claims 81-84, 86, 98, 100, 102 and103 have been considered but are moot in view of the new ground(s) of rejection.

Applicants argue that US '715 teaches adjusting pH to enhance the delivery of huperzine, and co-solvents are suggested as possibly improving the penetration of neutral forms of huperzine, and CN '987 teaches azone that cause skin irritation and excluded by the present claims.

In response to this argument, it is argued that a conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). US '715 and CN '987 suggested permeation enhancers, and according to the current rejection US '063 recognized fatty acids and fatty acid esters to enhance the delivery huperzine into the skin, and also taught the equivalency between fatty acids and their esters and azone in terms of skin enhancing effect, and this teaching of US '063 would have motivated one having ordinary skill in the art to include fatty acids and fatty acid esters into the transdermal delivery system disclosed by US '715 or CN '987.

Response to Amendment

10. The declaration under 37 CFR 1.132 filed 08/30/2007 is insufficient to overcome the rejection of claims 81-103 based upon obviousness over US '715 and CN '987 as set forth in the last Office action because: the combination of US '715 or CN '987 with

US '063 will teach the present invention as a whole. Further, the permeation enhancer used in the comparison (lauryl lactate) is not disclosed by applicants.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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